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Hypoglycaemic and Hypolipidaemic Effects of *Leptadenia hastata* (Pers.) Decne in Alloxan Induced Diabetic Rats

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ABSTRACT: *Laptadenia hastata* (Pers.) Decne. (Asclepiadaceae) is a widely distributed tropical African herb used as vegetable. It is also used traditionally in the management of diabetes mellitus and treatment of stomach ache. This study evaluated the hypoglycaemic and hypolipidaemic effects of water and methanol extracts of *L. hastata* in normal and alloxan-induced diabetic rats model. Oral administration of methanol and water extracts at 300 mg kg^{-1} body weight (bw) have significantly ($p < 0.05$) decreased the blood glucose and increased liver and muscle glycogen levels. Significant ($p < 0.05$) reduction of serum triglyceride, very low density lipoprotein cholesterol levels and an increase in high density lipoprotein cholesterol level were observed. The results of the current study have demonstrated the hypoglycaemic and hypolipidaemic effects of *L. hastata* extracts and underscore its potentials in the management of diabetes mellitus.
Keywords: Hypoglycaemia, hypolipidaemia, *Leptadenia hastata,*

INTRODUCTION

Diabetes is a wide spread metabolic disorder found in all populations throughout the world affecting between 5 to 10 % of the world population (Shaw *et al*., 2010). The prevalence rate of diabetes in Nigeria is estimated at 4.7 % with rural areas having the lowest rates (Shaw *et al*., 2010). Studies have shown that the cure for diabetes is currently unknown, but could adequately be managed by the use of agents that exhibit hypoglycemic effect. The most popular and effective of such agent is insulin. A good number of oral hypoglycaemic agents are also available, which includes sulphonylureas, biguanides and alpha glucosidase inhibitors (Tunbrige and Home, 1991). However, majority of these hypoglyceamic agents are either too expensive or their use is associated with some undesirable side effects and contraindications or both (Tunbrige and Home, 1991; Kameswara *et al*., 1999; Jouhari *et al*., 2000).

On the bases of the shortcomings and keeping in view the dangers associated with diabetic complications, some of which might results in premature death, the WHO study groups (WHO, 1985; 1994), has recommended among other things the need for the development and evaluation of better, safer and affordable pharmacological agents. The report further recommended the evaluation of the efficacy of traditional medicines and other non-pharmacological methods in use for the managements of the disease. Considering the above recommendations, interest in fostering research on plant products and screening for agents with hypoglycaemic agents is being pursued in various laboratories across the globe (WHO, 1985; 1994; Mei *et al*., 2005). Several medicinal plants have been used as dietary adjunct and in the treatment of numerous diseases without proper knowledge of their function. The multiple roles of wild traditional vegetables as both food and medicinal sources have widely been documented (Lee *et al*., 2003; Ogle *et al*., 2003; Adebooye and Opabode, 2004; Ayodele, 2005).

Leptadenia hastata belongs to the family asclepiadaceae widely used in Tropical Africa as vegetable (Burkil, 1985). The plant is medicinally important in the treatment of many ailments (Kerharo and Adams, 1974; Burkil, 1985; Oliver-Boyer, 1986; Aliero *et al*., 2001). Ethnobotanical information obtained from traditional medical

practitioners in northern Nigeria revealed that *L. hastata* is used for the treatment of diabetes mellitus. The antibacterial and antimicrobial effects of *L. hastata* have been reported (Aliero and Wara, 2009) and the result of its toxicity studies showed that the plant is relatively safe (Tambuora *et al*., 2005). There is however paucity of information confirming the claimed antidiabetic potential of *L. hastata*. The aim of this research is to evaluate the hypoglycaemic and hypolipidaemic potential of *L. hastata* with the view to validating its potentials in the management of diabetes mellitus.

MATERIALS AND METHODS

Collection of plant material and extracts preparation

Fresh leaves of *L. hastata* were collected from the Biological garden on the main Campus of the Usmanu Danfodiyo University Sokoto. The plant sample was authenticated at the Herbarium of Botany unit of the same Institution where voucher specimen No. UDUH/AB/ 0011060 was prepared and deposited. The leaves were allowed to air dry at room temperature and pulverized into fine powder. One hundred (100) grammes of the sample were separately extracted with methanol and water for 24 hr. The extracts were filtered and concentrated to dryness under reduced pressure. The percentage yield was calculated for each of the extract. The dried extracts obtained were screened for hypoglycaemic and hypolipidaemic effects using alloxan induced diabetic rat model.

Experimental Animals

Adult albino rats (Wister strains) of both sexes were used for this study. Apparently healthy rats were purchased from the Animal House of Usmanu Danfodiyo University, Sokoto. The rats were allowed to acclimatize to the environment and were maintained on standard laboratory diet and tap water *ad libitum* for a period of one week. The study was conducted with strict adherence to the ethical procedure on the use of animals for experiment.

Preparation of Diabetic Rats

The rats in the alloxan induced diabetic group were injected intraperitoneally with alloxan monohydrate, dissolved in sterile normal saline solution at a dose of 80 mg kg^{-1} bw /day for 3 days (Kato and Miura, 1994; Stanley *et al*., 2000). After a week from the last dose, rats with moderate hyperglyceamia with blood glucose range of 198-252 mg dl^{-1} (11-14 mM) were considered as diabetic and were used for the experiment (Pari and Maheswara, 1999; Jaouhari *et al*., 2000).

Experimental Design

The experimental animals were divided into four groups of eight rats: Group I – Normal Control (NC): rats received water only. Group II – Diabetic control (DC), Diabetic rats untreated. Group III – Diabetic rats treated with methanol extract (DTM), Diabetic rats treated with methanol extract of *L. hastata* (300 mg kg^{-1} bw) orally for seven days; Group IV – Diabetic rats treated with water extract (DTW), Diabetic rats treated with water extract of *L. hastata* (300 mg kg^{-1} bw oral route) for seven days.

Administration of Extracts

The treated groups in all cases were administered the extracts orally at 300 mg kg^{-1} bw per day in the morning hours for a week. The untreated groups in each case were administered 0.4 ml distilled water through the same route for a week. The animals in all cases were maintained on standard laboratory diet and tap water *ad libitum* throughout the period of experiment. The animals were weighed before the alloxan injection, at the beginning of the treatment and 24 h after the last treatment. After the last treatment, the rats were fasted for eight hours and anaesthetized by dropping each in a transparent plastic jar saturated with chloroform vapor. They were then removed from the jar. Blood samples were collected through cardiac puncture and placed into labelled centrifuge tubes to obtain sera. The liver and muscle tissues were collected.

Biochemical Parameters Determination

Serum glucose level was determined by the glucose oxidase method of Trinder (1969) using glucose GOD/PAP assay kits. The glycogen content of both the liver and skeletal muscle was determined by the method of Plummer (1987). Serum total cholesterol level was estimated by the enzymatic method of Allain *et al*. (1974), using cholesterol enzymatic endpoint method assay kit. Measurement of Serum High Density Lipoprotein

Cholesterol (HDL-C) was done by the method of Burstain *et al.* (1970). Measurement of Serum Triacylglycerol (TAG) was done by the method of Trinder (1969), employing triglycerides GPO-PAP assay kit. Serum low density lipoprotein cholesterol (LDL-C) and serum very low density lipoprotein cholesterol (VLDL-C) were calculated according to the Friedewald formula (Friedewald *et al.*, 1974) i. e LDL-C = TC - (HDL-C + TAG/5) and VLDL-C = TAG/5) respectively. Atherogenic index was calculated as the ratio of LDL-C to HDL-C. All the kits used in these assay were purchased from Randox Laboratories Ltd, UK.

Statistical Analysis

The results were expressed as mean ± standard deviation (SD), n = 8. The data were subjected to one-way analysis of variance (ANOVA) and differences between samples were determined by Waller Duncan's multiple range test using the Statistical Analysis System (SAS, 2003) program. P values < 0.05 were considered significant.

RESULTS

The percentage yield of methanol and water extracts of *L. hastata* leaf obtained was 11.4 and 31.5 % respectively. Changes in the body weights of normal and alloxan induced diabetic rats treated with methanol and water extracts of *L. hastata* leaf are presented in Table 1. The result indicate that alloxan had significantly ($p < 0.05$) decreased the body weight of the rats but administration of the extracts significantly increased the body weight of the rats.

Changes in serum glucose and tissue glycogen content of alloxan-induced diabetic rats treated with methanol and water extract of the leaf of *L. hastata* are presented in Table 2. The result indicate that the rats administered alloxan developed diabetes as evident from the significant ($p < 0.05$) elevation in blood glucose level when compared to normal control rats. A significant decreased in blood glucose level was observed in diabetic rats treated with methanol and water extracts. Liver and muscle tissue glycogen level decreased significantly ($p < 0.05$) in diabetic rats when compared to normal control rats. Administration of methanol and water extracts significantly ($p < 0.05$) increased the liver glycogen level, but not muscle tissue glycogen level.

Table 1: Effect of Methanol and Water Leaf Extracts of *L. hastata* on the Body Weight (g) of Alloxan induced Diabetic Rats

Period	Methanol extract	Water extract
Before alloxan injection	202.50 ± 28.52^{b}	208.04 ± 31.85^{b}
Seven days after alloxan injection	190.30 ± 15.30^{c}	195.80 ± 26.88^{c}
After treatment	206.50 ± 15.10^{a}	212.80 ± 17.10^{a}

*Values are mean ± standard deviation (n = 8), mean followed by different superscript in each column are significantly different ($p < 0.05$).

Table 2: Effect of Methanol and Water Leaf Extracts of *L. hastata* on Serum Glucose, Liver and Muscle Glycogen of Albino Rats.

Group	Glucose (mg/dl)	Liver glycogen (mg/g)	Muscle glycogen (mg/g)
Normal rats (Control)	97.50 ± 10.11^{c}	53.30 ± 3.63^{a}	14.80 ± 2.09^{a}
Diabetic rats (Control)	268.70 ± 10.46^{a}	14.8 ± 2.09^{c}	5.92 ± 2.09^{b}
Diabetic treated with methanol	103.32 ± 20.68^{c}	34.04 ± 5.54^{b}	10.36 ± 2.09^{ab}
Diabetic rats treated with water	133.16 ± 37.12^{b}	44.39 ± 3.61^{a}	11.84 ± 2.09^{a}

*Values are expressed as mean ± standard deviation (n= 8), means followed by different super script in a column are significantly ($p < 0.05$) different.

The lipid profile of rats treated with methanol and water leaf extracts of *L. hastata* are presented in Table 3. The result shows a significant increase ($p < 0.05$) in triglycerides and very low density lipoprotein cholesterol (VLDL-C) and a significant decrease ($p < 0.05$) in high density

lipoprotein cholesterol (HDL-C) levels in diabetic untreated rats. Administration of methanol and water extracts caused a significant decrease ($p < 0.05$) in triglycerides and VLDL-C levels and a significant increase ($p < 0.05$) in HDL-C level in diabetic treated rats. Despite the high levels of triglycerides in the diabetic untreated group, the atherogenic index (Aix) associated with all the experimental groups was very low.

Table 3: Effect of Methanol and Water Leaf Extracts of *L. hastata* on Serum Lipid Profile of Albino Rats.

Parameter	Normal (Control)	Diabetic (Control)	DTM	DTW
Total cholesterol	156.25 ± 10.08^{a}	102.08 ± 13.43^{c}	135.71 ± 16.94^{b}	127.50 ± 21.51^{b}
Triglyceride	106.40 ± 14.50^{c}	257.00 ± 22.32^{a}	187.40 ± 24.83^{b}	163.10 ± 20.69^{b}
HDL-C	41.50 ± 5.97^{a}	26.60 ± 3.84^{b}	41.90 ± 5.66^{a}	35.9 ± 4.74^{a}
LDL-C	94.14 ± 15.44^{a}	24.13 ± 18.04^{c}	56.25 ± 16.43^{b}	58.96 ± 30.44^{b}
VLDL-C	21.27 ± 3.17^{c}	51.40 ± 4.89^{a}	37.48 ± 5.36^{b}	32.68 ± 4.63^{b}
Aix	2.34 ± 0.66^{a}	0.96 ± 0.75^{b}	1.37 ± 0.44^{ab}	1.78 ± 1.17^{ab}

Values are mean ± standard deviation (n= 8) in mg/dl. Mean followed by different superscript in a raw are significantly ($p< 0.05$) different. DTM = Diabetic rats treated with methanol: DTW = Diabetes treated with water extract: HDL-C = High Density Lipoprotein Cholesterol: LDL-C= Low density lipoprotein cholesterol: VLDL-C = Very low density lipoprotein cholesterol.

DISCUSSION

Weight loss which is one of the clinical features of diabetes mellitus may be due to the degeneration of the adipocytes and muscle tissues to make up for the energy lost as a result of frequent urination and over conversion of glycogen to glucose. Weight loss is a very serious issue in the management of diabetes mellitus (Zink and Chaffin, 1998). In this study, the diabetic rats treated with methanol and water extracts showed a significant ($p < 0.05$) increase in body weights compared to the diabetic untreated groups which may be due to protein sparing effect. Several medicinal plants like *Carum carvi*, *Tinospora cordifolia, Gymnema sylvestre, Acacia chivalieri, Zizipus spina-christi, Arachis hypogaea* and *Solanum incanum, Albizzia chivalieri* (Shanmugasundram, 1990; Morelli and Zoorob, 2000; Bilbis *et al*., 2002; Ene *et al*., 2006; Saidu, 2010) showed weight reduction in alloxan diabetic rats.

The present study reports the hypoglycaemic effect of *L. hastata* leaf. The results indicate that both extracts reduce the blood glucose level in alloxan induced diabetic rats. The results are comparable with those obtained for *Albizzia chivalieri* (Saidu, 2010) and *Arachis hypogaea* (Bilbis *et al.,* 2002) in alloxan induced diabetic rats. The hypoglycaemic effects exhibited by *L. hastata* extracts could be linked to one or more mechanisms. The possible mechanism includes the stimulation of β-cells and subsequent release of insulin and activation of the insulin receptors. It may also be due to the enhancement of transport of blood glucose to the peripheral tissue. It can also be linked to the inhibition of the alpha-glucosidase activity (Babu *et al*., 2003).

Although, the liver though does not depend on insulin for glucose uptake, it depends on insulin for glucose utilization and it plays a pivotal role in glucose and lipid homeostasis. Decreased glycogenesis and increased gluconeogenesis are some of the changes associated with glucose metabolism in the diabetic liver (Baquer, 1998). Increase in liver glycogen can be brought about by an increase in glycogenesis and/or decrease in glycogenolysis (Babu *et al*., 2003). The activity exhibited by *L. hastata* extracts might be related to the stimulation of glycogenesis and/or inhibition of glycogenolysis in the diabetic rat liver which might be the case in the skeletal muscle tissue glycogen. Similar observation has been reported for the extracts of *Tinospora cordifolia* and *Gymnema sylvestre* by Shanmugasundram (1990).

The abnormal by high concentration of serum lipids in the diabetic subject is mainly due to increase in the mobilization of free fatty acids from the peripheral fat depots, since insulin

inhibits the hormone sensitive lipase (Pari and Latha, 2002). The marked hyperlipidaemia that characterizes the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots. Although an increase in serum TG and VLDL-C and a decrease in HDL-C were observed in this study, administration of methanol and water extracts of *L. hastata* to have corrected these abnormalities. Despite the high levels of triglycerides in the diabetic untreated group, the atherogenic index (Aix) associated with all the experimental groups were very low. The results of the current study demonstrate the hypoglycaemic and hypolipidaemic potential of *L. hastata* and could be a source of lead compounds in the management of diabetes mellitus.

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